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FITZPATRICK CELLA HARPER & SCINTO			MCCORMICK, MELENIE LEE	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/552,526	Applicant(s) KAMIYA ET AL.
	Examiner MELENIE MCCORMICK	Art Unit 1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on _____.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1.3-7.9-11, 18, 20-22 and 28-32 is/are pending in the application.
 - 4a) Of the above claim(s) 3, 18, 20-22 and 31 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1, 4-7, 9-11, 28-30 and 32 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)
 Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date _____
- 5) Notice of Informal Patent Application
- 6) Other: _____

DETAILED ACTION

Applicants' remarks with claim amendments submitted 08 December 2008 have been received and considered.

Claims 1, 3-7, 9-11, 18, 20-22, and 28-32 are pending.

Claims 3, 18, 20-22, and 31 stand withdrawn.

Claims 1, 4-7, 9-11, 28-30 and 32 are presented for examination on the merits.

The examiner examined 'leaves' as the alternative species on the merits.

Withdrawn Rejections

The previous claim objection has been withdrawn in light of the amendment to claim 1, which has been re-written and no longer requires 'a' after 'comprises'.

The previous claim objection to claim 8 is moot since claim 8 is cancelled.

The previous objection to Claims 4-5 and 9 is withdrawn in light of the amendment in which the claims have been re-written in proper multiple dependent form.

The previous rejection under 35 U.S.C. 112, second paragraph has been withdrawn in light of the amendment to claims 1 and 6, which now refer to the ingredients claimed in the alternative. In addition, the amendments to claims 7 and 8

which no longer recite "or the additive for food and drinks" overcome the rejection, as does the amendment to claim 7 omitting the term 'it'.

The previous rejection under 35 U.S.C. 112, first paragraph has been withdrawn in light of the amendments to the claims, which no longer recite prevention of arthritis and which are now drawn to Hydrangea macrophylla Seinge var Thunbergii Makino.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 5, 7-9-11, 28-30 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended claims now recite an agent for "delaying the onset of arthritis". The intended use of 'delaying the onset of arthritis' is not found in the specification as

originally filed. Therefore, it cannot be determined that Applicants were in possession of an agent for delaying the onset of arthritis at the time the Application was originally filed.

This is a new matter rejection.

Claims 1,4,5, 7, 9-11, 28-30 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an agent for treating arthritis which comprises as active ingredients leaves or branch ends of Hydrangea macrophylla Seringe var Thunbergii Makino or an extract of said leaves or branch ends and an amino sugar or salt thereof or glycosaminoglycan or a salt thereof, does not reasonably provide enablement for an agent for delaying the onset of arthritis which comprises as active ingredients leaves or branch ends of Hydrangea macrophylla Seringe var Thunbergii Makino or an extract of said leaves or branch ends and an amino sugar or salt thereof or glycosaminoglycan or a salt thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states,

"Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (Wands, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (Wands, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to an agent for treating or delaying the onset of arthritis which comprises, as active ingredients leaves or branch ends of Hydrangea macrophylla Seringe var Thunbergii Makino or an extract of said leaves or branch ends and an amino sugar or salt thereof or glycosaminoglycan or a salt thereof. Thus, the claims taken together with the specification imply that Applicants are claiming an agent which comprises leaves or branch ends of Hydrangea macrophylla Seringe var

Thunbergii Makino or an extract of said leaves or branch ends and an amino sugar or salt thereof or glycosaminoglycan or a salt thereof which treats or delays the onset of arthritis.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The state of the art is unpredictable with regard to arthritis. As referenced by Vikas Garg, M.D. (Arthritis Basics), the cause of most forms of arthritis is unknown (see e.g. page 7). Garg further provides risk factors that may increase the likelihood of developing arthritis, however, Garg also cautions that not everyone with the disease may exhibit risk factors and not everyone with risk factors will exhibit the disease (see e.g. page 7). Thus, it is clear that there is unpredictability with regard to arthritis. Garg also teaches that there is no certain way to prevent arthritis (see e.g. page 4, last paragraph). The state of the art is unpredictable concerning agents for treating arthritis. In addition, the state of the art of herbal medicine is unpredictable. As evidenced by Shaw et al., herbal remedies can have unpredictable adverse effects (see abstract). The use of glucosamine (an amino sugar) and chondroitin sulfate (a glycosaminoglycan) for treating osteoarthritis is modestly effective in relieving symptoms (see Walker- Abstract). Therefore the instantly claimed composition would be reasonably expected to offer some relief (i.e. treat) osteoarthritis. As discussed by Walker, however, evidence of natural remedies in chondroprotection was not established at the time of the instantly claimed invention.

(5) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided an example wherein a composition comprising an extract of *Hydrangea macrophylla*, glucosamine and chondroitin sulfate is effective in suppressing arthritis (see e.g. pages 37 and 40 of the instant specification). Applicants have not, however, demonstrated that the administration a composition comprising an extract of *Hydrangea macrophylla*, glucosamine and chondroitin sulfate protects against arthritis or delays the onset of arthritis, as instantly claimed.

(8) The quantity of experimentation necessary:

Considering the state of the art in arthritis treatments as discussed by Garg and Walker and the high unpredictability and the lack of guidance provided in the specification with regard to delaying the onset of arthritis using an agent comprising leaves or branch ends of *Hydrangea macrophylla* Seringe var *Thunbergii* Makino or an extract of said leaves or branch ends and an amino sugar or salt thereof or glycosaminoglycan or a salt thereof, one of ordinary skill in the art would be burdened with undue experimentation to determine the subjects in which arthritis inset could be delayed using an agent as instantly claimed.

Therefore, in view of the breadth of the claims encompassing a composition comprising leaves or branch ends of *Hydrangea macrophylla* Seringe var *Thunbergii* Makino or an extract of said leaves or branch ends and an amino sugar or salt thereof or glycosaminoglycan or a salt thereof which treats or delays the onset of arthritis, the lack of sufficient guidance or data or evidence supporting an arthritis delaying effect of

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the claimed composition, and the unpredictability in the art of treatment of arthritis and chondroprotection, as evidenced by Garg and Walker, one of skill in the art would find that undue experimentation would be required to practice the claimed invention.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 4-7, 9-11, 28-30 and 32 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sorgente et al. (US 6,162,787) in view of Guardia et al. (2001) in view of Balado (1953) and further in view of Matsuda et al. (1999) for the reasons set forth in the previous Office Action, which are restated below.

Sorgente et al. beneficially teach that oral administration of a composition comprising glucosamine or its salts and chondroitin sulfate (a type of glycosaminoglycan, as evidenced by applicant' claim 5) and/or its salts is effective for treating arthritis (see e.g. claims 1 and 29). Sorgente et al. further teaches that the

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arthritis may be osteoarthritis or rheumatoid arthritis (see e.g. claims 21-22). Sorgente et al. also teaches that the composition may contain auxiliary compounds, such as binders, vitamins, amino acids, fillers, gelatin, etc (see e.g. col 5, lines 51-57). Sorgente also discloses that the composition may be formulated as a tablet, capsule, suspension, aerosol spray and the like. A powder could be added to a food (i.e. a food additive) and a suspension reads on a drink.

Sorgente et al. does not explicitly teach that the composition additionally contains *Hydrangea macrophylla* or an extract thereof.

Guardia et al. beneficially teach that in an experimental model for inflammation, which is a suitable and simple model for evaluating potential anti-arthritis agents was used to determine the anti-inflammatory activity of flavonoids in adjuvant arthritis (see e.g. page 685-Discussion). Guardia et al. further teach that rutin was extremely effective in reducing inflammation (see e.g. page 685-Discussion). Guardia et al. further teach that the role of dietary flavonoids in the treatment of inflammatory diseases, such as rheumatoid arthritis is promising (see e.g. page 687).

Balado beneficially teaches that rutin was extracted and identified from the blossoms of *Hydrangea macrophylla* (see e.g. abstract).

Matsuda et al. beneficially teach that chemical constituents with anti-histamine activity were extracted from the leaves of *Hydrangea macrophylla* Seringe var. thunbergii Makino (see e.g. abstract).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to prepare a composition for use in treating arthritis

comprising an extract of *Hydrangea macrophylla*, glucosamine and chondroitin sulfate. A person of ordinary skill in the art would have had a reasonable expectation of success in doing so based upon teaching of Sorgente et al. that a composition comprising glucosamine or its salts and chondroitin sulfate and/or its salts is effective for treating arthritis (see e.g. claims 1 and 29). In addition, based upon the teaching of Balado that rutin is extracted from *Hydrangea macrophylla* and the teaching of Guardia et al. that rutin is extremely effective in reducing inflammation in a rat arthritis model and shows promise for treating arthritis, a person of ordinary skill in the art would have been motivated to extract *Hydrangea macrophylla* for the rutin contained therein and add this extract to other known anti-arthritis agents, such as glucosamine and chondroitin sulfate as taught by Sorgente et al. "The idea for combining them flows logically from their having been used individually in the prior art"; *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be *prima facie* obvious.). This rejection is based upon the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, See *In re Sussman*, 136 F.2d 715, 718, 58 USPQ 262, 264 (CCPA 1943). A person of ordinary skill in the art would have had a reasonable expectation of success in particularly using the variety *Hydrangea macrophylla* Seringe var. thunbergii Makino because this was a known variety at the time and was known to contain therapeutic chemical constituents. Therefore, since *Hydrangea macrophylla* Seringe var.

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thunbergii Makino is simply a variety of *Hydrangea macrophylla*, one of ordinary skill in the art would reasonably expect this variety, which is known to contain chemical constituents in the leaves, to contain rutin in the flowers, as disclosed by Balado. A person of ordinary skill in the art would have a reasonable expectation of success in optionally choosing a particular part of the plant for extraction, such as the leaves, since the leaves are known to contain useful chemical constituents. As previously stated, Sorgente et al. also disclose that the composition may be formulated as a tablet, capsule, suspension, aerosol spray and the like. A powder could be added to a food (i.e. a food additive) and a suspension reads on a drink. It would have therefore been obvious to one of ordinary skill in the art to formulate a composition comprising glucosamine, chondroitin sulfate and an extract *Hydrangea macrophylla* Seringe var. *thunbergii* Makino in these forms.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicants argue that there is no report that rutin is present in the leaves and branch ends of *Hydrangea macrophylla* Seringe var *thunbergii* Makino. Please note that the claims recite leaves or branch ends, not leaves and branch ends. Please also

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note that the species leaves was examined on the merits. With regard to the argument that there is no report that rutin is present in the leaves, this is understood. However, a person of ordinary skill in the art would have at least had a reasonable expectation of success in using the leaves to extract chemical constituents, since Matsuda et al. beneficially teach that useful chemical constituents were extracted from the leaves of *Hydrangea macrophylla* Seringe var. *thunbergii* Makino (see e.g. abstract). Therefore, although rutin itself is not disclosed, a person of ordinary skill in the art would reasonably expect that the leaves could contain useful compounds and would therefore be motivated to use the leaves to prepare an extract. Because Balado et al. teach that a compound known for being useful to treat arthritis is found the blossoms of *Hydrangea macrophylla* (see e.g. abstract), a person of ordinary skill in the art would at least be motivated to try a different aerial part the plant in an extract for use as an arthritic treatment, such as the leaves.

Applicants also argue that the present invention achieves unexpectedly superior results over the closest prior art and point to example 3 at pages 38-40 of the specification. This is not found persuasive. The decrease in the arthritic score for the claimed composition (group 4) is not greater than the additive effects of groups 2 and 3. As compared to group 1, group 2 results in 1.74 point decrease. As compared to group 1, group 3 results in a 1.0 point decrease. Using both compositions together, at least a 2.74 decrease would be expected. Group 4 results in a 2.74 point decrease. Therefore, the results are not unexpected. In addition, synergism is an unpredictable phenomenon, highly dependent upon specific proportions and/or amounts of particular ingredients.

The claims do not recite any amounts. Any mixture of the components embraced by the claims which does not exhibit an unexpected result (e.g. synergism) is therefore *ipso facto* unpatentable.

The rejection is therefore deemed proper and is maintained.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELENIE MCCORMICK whose telephone number is (571)272-8037. The examiner can normally be reached on M-F 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Patricia Leith/
Primary Examiner, Art Unit 1655